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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,326	12/22/2000	Koh Sato	04853.0052	9287

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,326	SATO ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6-16,19-21 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6-16,19-21 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 6, 13, 16 and 33 have been amended. Claims 17, 18 and 22-32 have been canceled. Claims 1, 4 and 6-16, 19-21 and 33 are pending and under consideration.

2. The rejection of claims 13-16, 19-21 and 32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of applicants amendment.

3. The rejection of claims 1, 4, 6-21 and 33 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in light of applicants amendment.

4. Claim 1 is drawn to a method for treating a patient suffering from or susceptible to hypercalcemic crisis associated with impaired consciousness comprising administering a humanized anti-PTH-rP antibody capable of inhibiting the binding between PTH-rP to a receptor thereof; decreasing and maintaining the blood calcium level by 1 mg/dl. Claim 33 embodies the method of claim [1] wherein the blood calcium level is decreased by at least 2 mg/dl. Potts teaches that when serum calcium levels are 15 mg/dl to 18 mg/dl or higher, coma and cardiac arrest can occur. A reduction of only 1 mg/dl or2 mg/dl at the minimum danger level of 15 mg/dl will not reduce the calcium level in the blood of said patient to the to the point at which the patient is out of danger for cardiac arrest and coma. Claim 13 is drawn to a method of treating a patient suffering from or susceptible to hypercalcemic crises associated with impaired consciousness comprising administering to a patient a humanized anti-PHT-rP antibody inhibiting the binding between PTH-rP and a receptor thereof, allowing the antibody to inhibit the binding of PTH-rP and "a" receptor thereof, decreasing a blood calcium level to at least 15 mg/dl to effectively treat the patient. Potts (cited above) teaches that when serum levels reach 15 to 18 mg /dl or higher, coma and cardiac arrest can occur. (page 1902). The recited limitation of decreasing the blood calcium level to 15 mg/dl does not decrease the calcium level to the point at which the patient is out of danger for cardiac arrest and coma. Thus, one of skill in the art would not be able to use the claimed method

5. Claims 1, 4, 9, 10, 12, 13-15, 19, 20 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seger et al (US 5,494,806) in view of Potts (Diseases of the Parathyroid gland and other Hyper- and Hypocalcemic Disorders, In: Harrison's principles of Internal Medicine, 12th Edition, pages 1902-1915, IDS reference) and Schlom (In: Molecular foundations of Oncology, Samuel Broader, Ed, 1991, pages 95-134).

Claim 1 is drawn to a method of treating hypercalcemic crisis associated with malignant tumor comprising administering a humanized anti-PTH-rP antibody capable of inhibiting the binding between PTH-rP to a receptor thereof; decreasing and maintaining the blood calcium level by 1 mg/dl within 24 hours to effectively treat the patient and maintaining the at least 1 mg/dl decrease in blood calcium level over at least 24 hours, wherein said blood calcium level decreases to below 15 mg/dl. Claim 4 embodies the method of claim 1 wherein the humanized anti-PTHrP antibody is an antibody fragment capable of inhibiting the binding between PTHrP and a receptor thereof. Claim 9 embodies the method of claim 1 wherein the hypercalcemic crises is associated with at least one of coma or cardiac arrest. Claim 10 embodies the method of claim 1 or claim 4 wherein the antibody is bound to the carrier. Claim 12 embodies the method of claim 4 fragment is Fab, scFv, F(ab')2 or Fv. Claim 33 embodies the method of claim 1 wherein the blood calcium level is decreased by at least 2 mg/dl

Claim 13 is drawn to a method of treating hypercalcemic crisis associated with malignant tumor comprising administering a humanized anti-PTH-rP antibody capable of inhibiting the binding between PTH-rP to a receptor thereof; decreasing the blood calcium level to below 15 mg/dl to effectively treat the patient. Claim 14 embodies the method of claim 13 wherein the patient is administered at least one fragment of the humanized anti-PTHrP antibody. Claim 15 embodies the method of claim 14 wherein the fragment is Fab, scFv, F(ab')2 or Fv. Claim 19 embodies the method of claim 13 wherein the hypercalcemic crises is associated with at least one of coma or cardiac arrest. Claim 20 embodies the method of claim 13 or 14, wherein the antibody is bound to a carrier.

Seger et al (U.S. 5,494,806) teach a method for rapidly intervening in a patient exhibiting hypercalcemia comprising the administration of antagonists of PTHrP (column 24, lines 35-41). Seger et al teach that such antagonists include compounds which interfere with the PTH receptor-mediated activation and that the appropriate antibody antagonist or peptide antagonist

is administered at a dosage that provides adequate competition for PTHrP binding to the PTH receptor and that this will correspond to the dosage sufficient to lower the calcium level to below 10 mg/dl (column 24, lines 41-51), thus fulfilling the specific embodiment of treating a patient susceptible to hypercalcemic crisis associated with impaired consciousness comprising administering to said patient a anti-PTHrP antibody inhibiting the binding between PTHrP and the PTH receptor and allowing the antibody to inhibit the binding of PTHrP to the PTH receptor and decreasing a blood calcium level to effectively treat said patient. Seger et al teach that the antibody can be formulated in a carrier (column 24, lines 45-46) thus fulfilling the specific embodiment of claims 10 and 20. Seger et al teach that treatment may be repeated as necessary for long term maintenance of acceptable calcium levels of less than 10.1 mg/dl (column 24, lines 52-55) thus fulfilling the specific embodiment of claims 1 and 13 specifying that the blood calcium level be decreased to below 15 mg/dl. Seger et al teach that the antibodies and other compounds of the invention are useful for the treatment of disorders characterized by the interaction between a cell receptor of the invention and a ligand (column 23, lines 25-40). Seger et al teach that hypercalcemia mediated by PTHrP results from humoral hypercalcemia of malignancy (column 23, lines 46-47) thus fulfilling the specific embodiment of claims 1 and 13 drawn to a malignant tumor. Seger et al teach that compounds, including antibodies and polypeptide, may be screened for their agonistic or antagonistic properties using the cAMP accumulation, intracellular calcium, and/or inositol phosphate assays as specifically described (columns 22, line 65-column 23, line 22). Seger et al do not specifically teach administering a humanized anti-PTHrP antibody or the treatment of hypercalcemic crises wherein the patient exhibits at least one of coma or cardiac arrest.

Potts teaches that severe hypercalcemia, usually defined as 15 mg/dl or above is a medical emergency, and that coma or cardiac arrest can occur when serum calcium levels are at 15 to 18 mg/dl or higher. Thus, the art recognizes that severe hypercalcemia results in coma or cardiac arrest.

Schlom teaches that in all of the previous reported human trials in which non-immunosuppressed patients were treated with multiple doses of murine antibodies only the first and perhaps the second dose of said antibody was efficiently reaching the tumor site due to the HAMA response. Schlom teaches that it is unrealistic to assume that just one or two

administrations of any anti-cancer therapeutic would be effective. Schlom teaches that the answer to this problem is the humanization of the murine antibodies (pages 97-98, bridging paragraph). Schlom also teaches that F(ab')2 or Fab' fragments also help reduce the HAMA response (page 119 second column, lines 16-17 under the heading "Single Chain Antigen Binding Proteins). Schlom also teaches that scFv although comparable in binding affinity to FAb' have a more rapid plasma clearance than the Fab' fragment resulting in a greater tumor to tissue ratio. Schlom also points out that the small size of the scFv improves the capacity for penetration through the tumor mass.. Schlom also points out that scFv are easier to make than F9ab')2 of Fab' fragments.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to treat a patient undergoing hypercalcemic crisis wherein said crises was manifest by coma or cardiac arrest or blood calcium levels in excess of 15 mg/dl by the administration of a humanized anti-PTHrP antibody which is an antagonist of PTHrP binding to the PTH receptor in order to lower blood calcium to normal levels. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Seger et al on the method of treating patients needing immediate intervention because elevated serum calcium level can be fatal; and the teachings of Potts regarding the risk of coma or cardiac arrest in individual having serum calcium levels of 15 mg/dl to 18 mg/ dl or higher. It would also be obvious to use a fragment of the antibody such as scFv for maximum penetration into the tumor vasculature. Further, one of skill in the art would be motivated to maintain the decrease in blood calcium levels in order insure that the patient was stabilized.

6. Claims 1, 4, 9-15, 19-21 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seger et al (US 5,494,806) and Potts (Diseases of the Parathyroid gland and other Hyper- and Hypocalcemic Disorders, In: Harrison's principles of Internal Medicine, 12th Edition, pages 1902-1915) and Schlom (In: Molecular foundations of Oncology, Samuel Broader, Ed, 1991, pages 95-134). as applied to claims 1, 4, 9, 10, 12, 13-15, 19, 20 and 33 above, and further in view of Gristina et al (5,681,565). The specific embodiments of claims 1, 4, 9, 10, 12, 13-15, 19, 20 and 33 and the teachings of Seger et al, Potts and Schlom which

render obvious said embodiments are set forth above. None of the cited reference specifically teach the antibody bound to the carrier PEG.

Gristina et al teach that antibodies can administered in a cream or ointment carrier such as oleaginous bases or polyethylene glycol for in situ use (column 5, lines 3-21).
It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention to use PEG as a carrier. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Grishina et al on the effectiveness of PEG as a carrier for in situ administration of antibodies.

7. Claims 1, 6, 9, 10, 13, 16, 19, 20 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the abstract of Sato et al (WO 9813388, IDS reference) in view of Potts (Diseases of the Parathyroid gland and other Hyper- and Hypocalcemic Disorders, In: Harrison's principles of Internal Medicine, 12th Edition, pages 1902-1915). The specific embodiments of claims 1, 6, 9, 10, 13, 16, 19, 20 and 33 are set forth above.

Claims 6 and 16 embody the methods of claim 1 and 13, respectively, wherein the antibody is humanized antibody deposited under the Accession Number FERM BP-5631, The specification teaches that the humanized monoclonal antibody #23-57-137-1 was deposited under the Accession Number FERM BP-5631. CHECK DEPOSIT
The abstract of Sato et al teaches the humanized #23-57-137-1 monoclonal antibody. The abstract teaches that the humanized antibody can be used to treat hypercalcemia and other disorders caused by cancer. The abstract does not teach that the humanized #23-57-137-1 monoclonal antibody would inhibit the binding of the PTHrP and the PTH receptor, however, the antibody is identical to the specific embodiment of claims 6 and 16, therefore said antibody must have the inherent characteristic of inhibiting the binding of PTHrP to the PTH receptor. The abstract does not specifically teach drug-resistant hypercalcemic crisis associated with coma and cardiac arrest of a blood calcium level in excess of 15mg/dl.

Potts teaches that severe hypercalcemia, usually defined as 15 mg/dl or above is a medical emergency, and that coma or cardiac arrest can occur when serum calcium levels are at 15 to 18 mg/dl or higher. Potts teaches that the humoral mediator of malignancy associated hypercalcemia is PTHrP. Potts teaches that this mediator competes with PTH for occupancy of

the PTH receptor and induces hypercalcemia in test animals, and that the data indicate that PTHrP acts through activation of the PTH receptor (page 1908, first column, lines 2-9). It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention to use the #23-57-137-1 antibody in the treatment of hypercalcemic crises. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Potts who describe hypercalcemic crises as resulting in coma or cardiac arrest. One of skill in the art would be motivated to provide an agent which would bind to PTHrP and decrease the binding of PTHrP to the PTH receptor because Potts teaches that it is the activation of the PTH receptor by PTHrP that is responsible for hypercalcemia. One of skill in the art would be motivated to combine the teachings of Potts with the teachings of Sato et al because the abstract of Sato et al states that the #23-57-137-1 antibody, which binds to PTHrP, can be used in the treatment of hypercalcemia. One of skill in the art would readily conclude that the that #23-57-137-1 would act by inhibiting the binding of PTHrP and the PTH receptor. Without being able to inhibit the binding of the PTHrP to the PTH receptor, the antibody would not be effective in the treatment of hypercalcemia, and the effect would not be consistent with the teachings of Sato et al, that the antibody is useful in treating hypercalcemia.

8. Claims 1, 4, 6, 9, 10, 12, 13-16, 19, 20 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the abstract of Sato et al (WO 9813388 and Potts (Diseases of the Parathyroid gland and other Hyper- and Hypocalcemic Disorders, In: Harrison's principles of Internal Medicine, 12th Edition, pages 1902-1915) as applied to claims 1, 6, 9, 10, 13, 16, 19, 20 and 33 above, and further in view of Schlom (In: Molecular foundations of Oncology, Samuel Broader, Ed, 1991, pages 95-134).

The combination of Sato et al and Potts renders obvious claims for the reasons set forth above. Claims 4 and 14 embody the methods of claims 1 and 13, respectively wherein the patient is administered at least one fragment of the humanized anti-PTHrP antibody. Claims 5 and 15 embody the method of claims 4 and 14, respectively wherein the fragment is chosen from at least one of Fab, scFV, F(ab')2 and Fv. Neither the abstract of Sato et al nor Potts et al teach the administration of antibody fragments.

9. Schlom teaches that F(ab')2 or Fab' fragments also help reduce the HAMA response (page 119 second column, lines 16-17 under the heading "Single Chain Antigen Binding Proteins). Schlom also teaches that scFv although comparable in binding affinity to Fab' have a more rapid plasma clearance than the Fab' fragment resulting in a greater tumor to tissue ratio. Schlom also points out that the small size of the scFv improves the capacity for penetration through the tumor mass.. Schlom also points out that scFv are easier to make than F9ab')2 of Fab' fragments.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention to use fragments of the #23-57-137-1 antibody in the treatment of hypercalcemic crises. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Schlom et al who point out that antibody fragments such as Fab' result in a greater tissue to tumor ration and that scFv have a greater ability to penetrate tumor vasculature.

10. Claims 1, 4, 6, 9, 10, 12, 13-16, 19, 20 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the abstract of Sato et al (WO 9813388) and Potts (Diseases of the Parathyroid Gland and Other Hyper- and Hypocalcemic Disorders, In: Harrison's principles of Internal Medicine, 12th Edition, pages 1902-1915) and Schlom (In: Molecular foundations of Oncology, Samuel Broader, Ed, 1991, pages 95-134).as applied to claims 1, 4, 6, 9, 10, 12, 13-16, 19, 20 and 33 above, and further in view of Gristina et al (US 5,681,565).
Claims 10 and 20 embody the methods of claims 1 or 4, or claims 13 or 14, respectively, wherein the antibody is bound to a carrier. Claims 11 and 21 specify that the carrier of claim 31 is PEG. Neither of the prior art references of the Sato et al abstract, nor Potts, nor Schlom teach antibodies bound to PEG as a carrier.

Gristina et al teach that antibodies can administered in a cream or ointment carrier such as oleaginous bases or polyethylene glycol for in situ use (column 5, lines 3-21).
It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention to use PEG as a carrier for the #23-57-137-1 antibody. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Grishina et al on the effectiveness of PEG as a carrier for in situ administration of antibodies.

11. Claims 1, 4 and 6-16, 19-21 and 33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 126-136 and 138 of copending Application No. 09/269,332 in view of Potts (Diseases of the Parathyroid gland and other Hyper- and Hypocalcemic Disorders, In: Harrison's principles of Internal Medicine, 12th Edition, pages 1902-1915) and Schlom (In: Molecular foundations of Oncology, Samuel Broader, Ed, 1991, pages 95-134).

Claims 126-136 and 138 of the '332 application teach the administration of a polypeptide comprising an L chain V region of a humanized antibody comprising an amino acid sequence selected from the group consisting of SEQ ID NO:48-51 or 52-55.

Potts teaches that severe hypercalcemia, usually defined as 15 mg/dl or above is a medical emergency, and that coma or cardiac arrest can occur when serum calcium levels are at 15 to 18 mg/dl or higher.

Schlom teaches that F(ab')2 or Fab' fragments also help reduce the HAMA response (page 119 second column, lines 16-17 under the heading "Single Chain Antigen Binding Proteins). Schlom also teaches that scFv although comparable in binding affinity to FAb' have a more rapid plasma clearance than the Fab' fragment resulting in a greater tumor to tissue ratio. Schlom also points out that the small size of the scFv improves the capacity for penetration through the tumor mass.. Schlom also points out that scFv are easier to make than F9ab')2 of Fab' fragments.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to treat a patient undergoing hypercalcemic crisis wherein said crises was manifest by coma or cardiac arrest by carrying out the methods of claims 126-136 and 138 in order to lower blood calcium to normal levels. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Potts regarding the risk of coma or cardiac arrest in individual having serum calcium levels of 15 mg/dl to 18 mg/ dl or higher. It would also be obvious to use a fragment of the antibody such as scFv for maximum penetration into the tumor vasculature.

It is noted that claims 126-136 and 138 do not specify the administration of a humanized #23-57-137-1 antibody. However, said antibody is included in the genus of antibodies upon which the '332 method claims depend. The Office does not have the facilities and resources to

provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).
This is a provisional obviousness-type double patenting rejection.

14. Claims 1, 4 and 6-16, 19-21 and 33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 126-136 and 138 of copending Application No. 09/269, and Potts (Diseases of the Parathyroid gland and other Hyper- and Hypocalcemic Disorders, In: Harrison's principles of Internal Medicine, 12th Edition, pages 1902-1915) and Schlom (In: Molecular foundations of Oncology, Samuel Broader, Ed, 1991, pages 95-134) as applied to claims 22-30 above and in further view of Gristina et al (US 5,681,565).

Gristina et al teach that antibodies can administered in a cream or ointment carrier such as oleaginous bases or polyethylene glycol for in situ use (column 5, lines 3-21).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention to use PEG as a carrier for the antibodies in method claims 126-136 and 138 of application '322. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Grishina et al on the effectiveness of PEG as a carrier for in situ administration of antibodies.

12. Applicant has amended claims 1, 4 and 6-16, 19-21 and 33 in order that one of skill in the art can make and use the instant invention. However, because of said amendment the instant claims are now obvious over the prior art.

13. All other rejections and objections as set forth in the previous Office action are withdrawn.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

KAREN [illegible] PRIMARY EXAMINER

7/27/2004

Karen A. Canella

KAREN A. CANELLA PH.D
PRIMARY EXAMINER